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NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	JAN 27	Source of Registration (SR) information in REGISTRY updated and searchable
NEWS	4	JAN 27	A new search aid, the Company Name Thesaurus, available in CA/CAplus
NEWS	5	FEB 05	German (DE) application and patent publication number format changes
NEWS	6	MAR 03	MEDLINE and LMEDLINE reloaded
NEWS	7	MAR 03	MEDLINE file segment of TOXCENTER reloaded
NEWS	8	MAR 03	FRANCEPAT now available on STN
NEWS	9	MAR 29	Pharmaceutical Substances (PS) now available on STN
NEWS	10	MAR 29	WPIFV now available on STN
NEWS	11	MAR 29	No connect hour charges in WPIFV until May 1, 2004
NEWS	12	MAR 29	New monthly current-awareness alert (SDI) frequency in RAPRA
NEWS	13	APR 26	PROMT: New display field available
NEWS	14	APR 26	FIPAT/IFIUDB/IFICDB: New super search and display field available
NEWS	15	APR 26	LITALERT now available on STN
NEWS	16	APR 27	NLDB: New search and display fields available

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=> s retigabine or d 23129 or 150812-12-7/rn
'RN' IS NOT A VALID FIELD CODE
'RN' IS NOT A VALID FIELD CODE
'RN' IS NOT A VALID FIELD CODE
L1          375 RETIGABINE OR D 23129 OR 150812-12-7/RN

=> s l1 and (pain or non-inflammatory or noninflammatory)
L2           47 L1 AND (PAIN OR NON-INFLAMMATORY OR NONINFLAMMATORY)

=> dup rem l2
PROCESSING COMPLETED FOR L2
L3           28 DUP REM L2 (19 DUPLICATES REMOVED)

=> focus
PROCESSING COMPLETED FOR L3
L4           28 FOCUS L3 1-

=> d ibib abs 1-28

L4   ANSWER 1 OF 28  CAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         2000:636213  CAPLUS
DOCUMENT NUMBER:          133:187979
TITLE:                    Use of retigabine for the treatment of
                          pain
INVENTOR(S):              Rundfeldt, Chris; Bartsch, Reni; Rostock, Angelika;
                          Tober, Christine; Dost, Rita
PATENT ASSIGNEE(S):       ASTA Medica Aktiengesellschaft, Germany
SOURCE:                   U.S., 5 pp.
                          CODEN: USXXAM
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.         KIND  DATE           APPLICATION NO.  DATE
     ---------------    ----  --------       ---------------  --------
     US 6117900          A    20000912       US 1999-406135   19990927
     WO 2001022953       A2   20010405       WO 2000-EP9284   20000922
     WO 2001022953       A3   20020523
         W:  AU, BG, BR, BY, CA, CN, CZ, EE, GE, HR, HU, ID, IL, IN, IS, JP,
             KG, KR, KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR,
             UA, UZ, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
             PT, SE
     BR 2000014293       A    20020521       BR 2000-14293    20000922
     EP 1223927          A2   20020724       EP 2000-969283   20000922
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY
```

NZ 517616	A	20021220	NZ 2000-517616		20000922
JP 2003510273	T2	20030318	JP 2001-526165		20000922
EE 200200145	A	20030415	EE 2002-145		20000922
BG 106450	A	20020930	BG 2002-106450		20020227
HR 2002000234	A1	20030630	HR 2002-234		20020318
NO 2002001418	A	20020321	NO 2002-1418		20020321
ZA 2002002449	A	20030128	ZA 2002-2449		20020327
PRIORITY APPLN. INFO.:			US 1999-406135	A	19990927
			WO 2000-EP9284	W	20000922

AB The invention relates to the use of 2-amino-4-(4-fluorobenzylamino)-1-ethoxycarbonylaminobenzene (**retigabine**), or a pharmaceutically utilizable salt thereof, for the prophylaxis and treatment of **pain**, e.g. neuropathic **pain**.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:65295 CAPLUS

DOCUMENT NUMBER: 139:46967

TITLE: The anticonvulsant **retigabine** attenuates nociceptive behaviours in rat models of persistent and neuropathic **pain**

AUTHOR(S): Blackburn-Munro, Gordon; Jensen, Bo Skaaning

CORPORATE SOURCE: Department of Pharmacology, NeuroSearch A/S, Ballerup, DK-2750, Den.

SOURCE: European Journal of Pharmacology (2003), 460(2-3), 109-116
CODEN: EJPHAZ; ISSN: 0014-2999

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We have tested for anti-nociceptive effects of the anticonvulsant KCNQ channel opener, N-(2-amino-4-(4-fluorobenzylamino)-phenyl)carbamic acid Et ester (**retigabine**), in rat models of exptl. **pain**. In the chronic constriction injury and spared nerve models of neuropathic **pain**, injection of **retigabine** (5 and 20 mg/kg, p.o.) significantly attenuated ($P<0.05$) mech. hypersensitivity in response to pin prick stimulation of the injured hindpaw. In contrast, **retigabine** had no effect on mech. hypersensitivity to von Frey stimulation of the injured hindpaw in either model. Cold sensitivity in response to Et chloride was only attenuated ($P<0.05$) in the chronic constriction injury model. In the formalin test, **retigabine** (20 mg/kg, p.o.) attenuated flinching behavior in the second phase compared with vehicle ($P<0.05$), and this effect was completely reversed by the KCNQ channel blocker 10,10-bis(4-pyridinylmethyl)-9(10H)-anthracenone (XE-991; 3 mg/kg, i.p.). Neither **retigabine** nor XE-991 administration affected the latency to respond to noxious thermal stimulation of the tail in control animals. These results suggest that **retigabine** may prove to be effective in the treatment of neuropathic **pain**.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:690613 CAPLUS

DOCUMENT NUMBER: 140:87016

TITLE: Lack of pharmacokinetic interaction between **retigabine** and phenobarbitone at steady-state in healthy subjects

AUTHOR(S): Ferron, Geraldine M.; Patat, Alain; Parks, Virginia; Rolan, Paul; Troy, Steven M.

CORPORATE SOURCE: Clinical Pharmacology Department, Wyeth Research, Collegeville, PA, USA

SOURCE: British Journal of Clinical Pharmacology (2003), 56(1), 39-45

CODEN: BCPHBM; ISSN: 0306-5251
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To evaluate potential pharmacokinetic interactions between phenobarbitone and **retigabine**, a new antiepileptic drug. Fifteen healthy men received 200 mg of **retigabine** on day 1. On days 432, phenobarbitone 90 mg was administered at 22.00 h. On days 26-32, increasing doses of **retigabine** were given to achieve a final dose of 200 mg every 8 h on day 32. The pharmacokinetics of **retigabine** were determined on days 1 and 32, and those for phenobarbitone on days 25 and 31. After administration of a single 200 mg dose, **retigabine** was rapidly absorbed and eliminated with a mean terminal half-life of 6.7 h, a mean AUC of 3936 ng ml-' h and a mean apparent clearance of 0.761 h-1 kg-1. Similar exposure to the partially active acetylated metabolite (AWD21-360) of **retigabine** was observed After administration of phenobarbitone dosed to steady-state, the pharmacokinetics of **retigabine** at steady-state were similar (AUC of 4433 ng ml-1 h and t1/2 of 8.5 h) to those of **retigabine** alone. The AUC of phenobarbitone was 298 mg l-1 h when administered alone and 311 mg ml-1 h after **retigabine** administration. The geometric mean ratios and 90% confidence intervals of the AUC were 1.11 (0.97, 1.28) for **retigabine**, 1.01 (0.88, 1.06) for AWD21-360 and 1.04 (0.96, 1.11) for phenobarbitone. Individual and combined treatments were generally well tolerated. One subject was withdrawn from the study on day 10 due to severe abdominal **pain**. Headache was the most commonly reported adverse event. No clin. relevant changes were observed in the electrocardiograms, vital signs or laboratory measurements. There was no pharmacokinetic interaction between **retigabine** and phenobarbitone in healthy subjects. No dosage adjustment is likely to be necessary when **retigabine** and phenobarbitone are coadministered to patients.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:389379 CAPLUS
DOCUMENT NUMBER: 135:221181
TITLE: KCNQ4 channel activation by BMS-204352 and **retigabine**
AUTHOR(S): Schroder, R. L.; Jespersen, T.; Christophersen, P.; Strobaek, D.; Jensen, B. S.; Olesen, S.-P.
CORPORATE SOURCE: NeuroSearch A/S, Ballerup, DK 2750, Den.
SOURCE: Neuropharmacology (2001), 40(7), 888-898
CODEN: NEPHBW; ISSN: 0028-3908
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Activation of potassium channels generally reduces cellular excitability, making potassium channel openers potential drug candidates for the treatment of diseases related to hyperexcitability such as epilepsy, neuropathic **pain**, and neurodegeneration. Two compds., BMS-204352 and **retigabine**, presently in clin. trials for the treatment of stroke and epilepsy, resp., have been proposed to exert their protective action via an activation of potassium channels. Here we show that KCNQ4 channels, stably expressed in HEK293 cells, were activated by **retigabine** and BMS-204352 in a reversible and concentration-dependent manner in the concentration range 0.1-10 μM. Both compds. shifted the KCNQ4 channel activation curves towards more neg. potentials by about 10 mV. Further, the maximal current obtainable at large pos. voltages was also increased concentration-dependently by both compds. Finally, a pronounced slowing of the deactivation kinetics was induced in particular by BMS-204352. The M-current blocker linopirdine inhibited the baseline current, as well as the BMS-204352-induced activation of the KCNQ4

channels. KCNQ2, KCNQ2/Q3, and KCNQ3/Q4 channels were activated to a similar degree as KCNQ4 channels by 10 μM of BMS-204352 and **retigabine**, resp. The compds. are, thus, likely to be general activators of M-like currents.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:283501 CAPLUS

TITLE: The anti-hyperalgesic activity of **retigabine** is mediated by KCNQ potassium channel activation

AUTHOR(S): Dost, R.; Rostock, A.; Rundfeldt, C.

CORPORATE SOURCE: elbion AG, Meissner Strasse 191, Radebeul, 01445, Germany

SOURCE: Naunyn-Schmiedeberg's Archives of Pharmacology (2004), 369(4), 382-390
CODEN: NSAPCC; ISSN: 0028-1298

PUBLISHER: Springer-Verlag

DOCUMENT TYPE: Journal

LANGUAGE: English

AB **Retigabine** (N-(2-amino-4-(4-fluorobenzylamino)-phenyl) carbamic acid Et ester) has a broad anticonvulsant spectrum and is currently in clin. development for epilepsy. The compound has an opening effect on neuronal KCNQ channels. At higher concns. an augmentation of gamma-aminobutyric acid (GABA) induced currents as well as a weak blocking effect on sodium and calcium currents were observed The goal of this study was to characterize the activity of **retigabine** in models of acute and neuropathic **pain** and to investigate if the potassium channel opening effect of **retigabine** contributes to its activity. **Retigabine** was tested in mice and rats in the tail flick model of acute **pain** and in the nerve ligation model with tight ligation of the 5th spinal nerve (L5) using both thermal and tactile stimulation. While **retigabine** like gabapentin had almost no analgesic effect in mice it showed some analgesic effects in rats in the tail flick model. These effects could not be antagonized with linopirdine, a selective KCNQ potassium channel blocker, indicating a different mode of action for this activity. In L5-ligated rats **retigabine** significantly and dose-dependently elevated the **pain** threshold and prolonged the withdrawal latency after tactile and thermal stimulation, resp. In the L5 ligation model with thermal stimulation **retigabine** 10 mg/kg p.o. was as effective as 100 mg/kg gabapentin or 10 mg/kg tramadol. The L5 model with tactile stimulation was used to test the role of the KCNQ potassium channel opening effect of **retigabine**. If **retigabine** 10 mg/kg p.o. was administered alone it was as effective as tramadol 10 mg/kg p.o. in elevating the **pain** threshold. Linopirdine (1 and 3 mg/kg i.p.) had nearly no influence on neuropathic **pain** response. If we administered both **retigabine** and linopirdine the effect of **retigabine** was abolished or diminished depending on the dose of linopirdine used. In summary, **retigabine** is effective in predictive models for neuropathic **pain**. The activity is comparable to tramadol and is present at lower doses compared with gabapentin. Since the anti-allodynic effect can be inhibited by linopirdine we can conclude that the potassium channel opening properties of **retigabine** are critically involved in its ability to reduce neuropathic **pain** response.

L4 ANSWER 6 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:638248 CAPLUS

DOCUMENT NUMBER: 140:53256

TITLE: KCNQ/M currents in sensory neurons: Significance for **pain** therapy

AUTHOR(S): Passmore, Gayle M.; Selyanko, Alexander A.; Mistry, Mohini; Al-Qatari, Mona; Marsh, Stephen J.; Matthews,

Elizabeth A.; Dickenson, Anthony H.; Brown, Terry A.; Burbidge, Stephen A.; Main, Martin; Brown, David A.
CORPORATE SOURCE: Department of Pharmacology, University College London, London, WC1E 6BT, UK
SOURCE: Journal of Neuroscience (2003), 23(18), 7227-7236
CODEN: JNRSDS; ISSN: 0270-6474
PUBLISHER: Society for Neuroscience
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Neuronal hyperexcitability is a feature of epilepsy and both inflammatory and neuropathic **pain**. M currents [IK(M)] play a key role in regulating neuronal excitability, and mutations in neuronal KCNQ2/3 subunits, the mol. correlates of IK(M), have previously been linked to benign familial neonatal epilepsy. Here, we demonstrate that KCNQ/M channels are also present in nociceptive sensory systems. IK(M) was identified, on the basis of biophys. and pharmacol. properties, in cultured neurons isolated from dorsal root ganglia (DRGs) from 17-d-old rats. Currents were inhibited by the M-channel blockers linopirdine (IC50, 2.1 μM) and XE991 (IC50, 0.26 μM) and enhanced by **retigabine** (10 μM). The expression of neuronal KCNQ subunits in DRG neurons was confirmed using reverse transcription-PCR and single-cell PCR anal. and by immunofluorescence. **Retigabine**, applied to the dorsal spinal cord, inhibited C and Aδ fiber-mediated responses of dorsal horn neurons evoked by natural or elec. afferent stimulation and the progressive "windup" discharge with repetitive stimulation in normal rats and in rats subjected to spinal nerve ligation. **Retigabine** also inhibited responses to intrapaw application of carrageenan in a rat model of chronic **pain**; this was reversed by XE991. It is suggested that IK(M) plays a key role in controlling the excitability of nociceptors and may represent a novel analgesic target.

REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 28 USPATFULL on STN
ACCESSION NUMBER: 2002:283127 USPATFULL
TITLE: Modulatory binding site in potassium channels for screening and finding new active ingredients
INVENTOR(S): Rundfeldt, Chris, Coswig, GERMANY, FEDERAL REPUBLIC OF
Netzer, Rainer, Hamburg, GERMANY, FEDERAL REPUBLIC OF
PATENT ASSIGNEE(S): Arzneimittelwerk Dresden GmbH, Radebeul, GERMANY, FEDERAL REPUBLIC OF (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6472165	B1	20021029	
APPLICATION INFO.:	US 1999-368314		19990803	(9)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Guzo, David
ASSISTANT EXAMINER: Leffers, Jr., Gerald G.
LEGAL REPRESENTATIVE: Fulbright & Jaworski L.L.P.
NUMBER OF CLAIMS: 11
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 0 Drawing Figure(s); 0 Drawing Page(s)
LINE COUNT: 611
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A selective modulatory **retigabine** binding potassium channel receptor site containing subunits KCNQ2 and KCNQ3, and a method for directly selectively modulating that receptor site by administering **retigabine** to a cell preparation of the potassium channel.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 8 OF 28 USPATFULL on STN

ACCESSION NUMBER: 2003:238492 USPATFULL
TITLE: Cinnamide derivatives as KCNQ potassium channel modulators
INVENTOR(S): Wu, Yong-Jin, Madison, CT, UNITED STATES
Sun, Li-Quang, Glastonbury, CT, UNITED STATES
Chen, Jie, Madison, CT, UNITED STATES
He, Huan, Wallingford, CT, UNITED STATES
L'Heureux, Alexandre, Longueuil, CANADA
Dextraze, Pierre, Laprairie, CANADA
Daris, Jean-Paul, St. Hubert, CANADA
Kinney, Gene G., Collegeville, PA, UNITED STATES
Dworetzky, Steven I., Middlefield, CT, UNITED STATES
Hewawasam, Piyasena, Middletown, CT, UNITED STATES

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2003166650	A1	20030904	
APPLICATION INFO.:	US 2002-160582	A1	20020531	(10)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2001-294815P	20010531	(60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: STEPHEN B. DAVIS, BRISTOL-MYERS SQUIBB COMPANY, PATENT DEPARTMENT, P O BOX 4000, PRINCETON, NJ, 08543-4000
NUMBER OF CLAIMS: 28
EXEMPLARY CLAIM: 1
LINE COUNT: 4774
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB There is provided novel cinnamide derivatives of Formula I ##STR1##

wherein R is C.sub.1-4 alkyl or trifluoromethyl; R.sup.1 is selected from the group consisting of pyridinyl, quinolinyl, thienyl, furanyl, 1,4-benzodioxanyl, 1,3-benzodioxolyl, chromanyl, indanyl, biphenylyl, phenyl and substituted phenyl in which said substituted phenyl is substituted with one or two substituents each independently selected-from the group consisting of halogen, C.sub.1-4 alkyl, C.sub.1-4 alkoxy, trifluoromethyl, trifluoromethoxy and nitro; R.sup.2 and R.sup.3 are each independently selected from the group consisting of hydrogen, C.sub.1-4 alkyl, and halogen; R.sup.4 is selected from the group consisting of di(C.sub.1-4 alkyl)amino, trifluoromethoxy and optionally substituted morpholin-4-yl, pyridinyl, pyrimidinyl, piperazinyl, and pyrazinyl with one or two substituents in which said substituent is independently selected from the group consisting of C.sub.1-4 alkyl, aminomethyl, hydroxymethyl, chloro or fluoro; R.sup.5 is hydrogen, chloro or fluoro; or R.sup.4 and R.sup.5 taken together are --CH.dbd.CH--CH.dbd.CH-- or --X(CH.sub.2).sub.mY-- in which X and Y are each independently selected from the group consisting of CH.sub.2, (CH.sub.2).sub.nN(R.sup.9)-- and O, wherein m is 1 or 2; n is 0 or 1; and R.sup.6, R.sup.7, and R.sup.8 are each independently selected from hydrogen, chloro and fluoro; and R.sup.9 is selected from the group consisting of hydrogen, C.sub.1-4 alkyl, hydroxyethyl, C.sub.1-4 alkoxyethyl, cyclopropylmethyl, --CO.sub.2(C.sub.1-4alkyl), and --CH.sub.2CH.sub.2NR.sup.10R.sup.11 in which R.sup.10 and R.sup.11 are each independently hydrogen or C.sub.1-4 alkyl, which are openers of the KCNQ potassium channels and are useful in the treatment of disorders which are responsive to the opening of the KCNQ potassium channels.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 9 OF 28 USPATFULL on STN
ACCESSION NUMBER: 2002:323226 USPATFULL
TITLE: Methods for treating hyperactive gastric motility

INVENTOR(S): Argentieri, Thomas M., Yardley, PA, UNITED STATES
PATENT ASSIGNEE(S): Wyeth, Madison, NJ (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002183395	A1	20021205
APPLICATION INFO.:	US 2002-114148	A1	20020402 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-281471P	20010404 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: George M. Tarnowski, 5 Giralda Farms, Madison, NJ, 07940
NUMBER OF CLAIMS: 23
EXEMPLARY CLAIM: 1
LINE COUNT: 719
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides methods and pharmaceutical compositions for treating, inhibiting or preventing hyperactive gastric motility in a mammal utilizing agonists of KCNQ potassium channels, including KCNQ2, KCNQ3, KCNQ4 and KCNQ5 potassium channels, alone or in combination. The hyperactive gastric motility may be associated with maladies including, colitis, irritable bowel syndrome and Crohn's disease. Compounds useful in these methods include the 1,2,4-triamino-benzene derivatives described in U.S. Pat. Number 5,384,330 (Dieter et al.) and the substituted 3-phenyl oxindole compounds described in U.S. Pat. Number 5,565,483 (Hewawasam et al.). Among the preferred compounds of this invention is N-[2-amino-4-(4-fluorobenzylamino)-phenyl]carbamic acid ethyl ester, also referred to as **retigabine**.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 10 OF 28 USPATFULL on STN
ACCESSION NUMBER: 2002:236079 USPATFULL
TITLE: Modulators of KCNQ potassium channels and use thereof in treating migraine and mechanistically related diseases
INVENTOR(S): Dworetzky, Steven I., Middlefield, CT, UNITED STATES
Gribkoff, Valentin K., Wallingford, CT, UNITED STATES
Kinney, Gene G., Collegeville, PA, UNITED STATES
Hewawasam, Piyasena, Middletown, CT, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002128277	A1	20020912
APPLICATION INFO.:	US 2002-75703	A1	20020214 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-269967P	20010220 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Stephen B. Davis, BRISTOL-MYERS SQUIBB COMPANY, Patent Department, P. O. Box 4000, Princeton, NJ, 08543-4000
NUMBER OF CLAIMS: 16
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 7 Drawing Page(s)
LINE COUNT: 1482
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds which function as modulators, particularly, openers, of human KCNQ potassium channel proteins or polypeptides, particularly, central nervous system (CNS)-located KCNQ potassium channels, and

heteromultimers thereof, and their use in the treatment of migraine are provided by the present invention. One novel type of potassium channel polypeptide openers provided by the present invention is the fluorooxindole compounds, described for the first time as therapeutics for the treatment of migraine by preventing the asynchronous firing of neurons. Other KCNQ potassium channel opener compounds that are also useful in the treatments of the invention include 2,4-disubstituted pyrimidine-5-carboxamide derivatives. One or more of the compounds according to the present invention may be utilized alone, in combination, or in conjunction with other treatment modalities for reducing, ameliorating and/or alleviating migraine or diseases similar to, or mechanistically related to, migraine, e.g., cluster headache.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 11 OF 28 USPATFULL on STN
ACCESSION NUMBER: 2004:39407 USPATFULL
TITLE: Methods for treating hyperactive gastric motility
INVENTOR(S): Argentieri, Thomas M., Yardley, PA, UNITED STATES
PATENT ASSIGNEE(S): Wyeth, Madison, NJ, UNITED STATES (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004029949	A1	20040212
APPLICATION INFO.:	US 2003-635081	A1	20030806 (10)

RELATED APPLN. INFO.: Division of Ser. No. US 2002-114148, filed on 2 Apr 2002, ABANDONED

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-281471P	20010404 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: WYETH, PATENT LAW GROUP, FIVE GIRALDA FARMS, MADISON, NJ, 07940
NUMBER OF CLAIMS: 6
EXEMPLARY CLAIM: 1
LINE COUNT: 629
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides methods and pharmaceutical compositions for treating, inhibiting or preventing hyperactive gastric motility in a mammal utilizing agonists of KCNQ potassium channels, including KCNQ2, KCNQ3, KCNQ4 and KCNQ5 potassium channels, alone or in combination. The hyperactive gastric motility may be associated with maladies including, colitis, irritable bowel syndrome and Crohn's disease. Compounds useful in these methods include the 1,2,4-triamino-benzene derivatives described in U.S. Pat. Number 5,384,330 (Dieter et al.) and the substituted 3-phenyl oxindole compounds described in U.S. Pat. Number 5,565,483 (Hewawasam et al.).

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 12 OF 28 USPATFULL on STN
ACCESSION NUMBER: 2003:258454 USPATFULL
TITLE: Use of 3-substituted oxindole derivatives as kcnq potassium channel modulators
INVENTOR(S): Jensen, Bo Skaaning, Ballerup, DENMARK
Schroder, Rikke, frederiksberg, DENMARK
Strobaek, Dorte, Ballerup, DENMARK
Olesen, Soren Peter, Ballerup, DENMARK

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003181507	A1	20030925

APPLICATION INFO.: US 2003-312123 A1 20030224 (10)
WO 2001-DK412 20010614

	NUMBER	DATE
PRIORITY INFORMATION:	DK 2000-1022	20000629
	DK 2001-394	20010308

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: BIRCH STEWART KOLASCH & BIRCH, PO BOX 747, FALLS CHURCH, VA, 22040-0747
NUMBER OF CLAIMS: 9
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 4 Drawing Page(s)
LINE COUNT: 762
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to a novel method of treating of **pain** or anxiety, using compounds that modulate KCNQ potassium channels and currents. ##STR1##

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 13 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:933608 CAPLUS
TITLE: The therapeutic potential of neuronal KCNQ channel modulators
AUTHOR(S): Gribkoff, Valentin K.
CORPORATE SOURCE: Department 401, Neuroscience Drug Discovery, Bristol-Myers Squibb Pharmaceutical Research Institute, Wallingford, CT, 06492, USA
SOURCE: Expert Opinion on Therapeutic Targets (2003), 7(6), 737-748
CODEN: EOTTAO; ISSN: 1472-8222
PUBLISHER: Ashley Publications Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Neuronal KCNQ (Kv7) channels (KCNQ2 - 5 or Kv7.2 - 7.5, disclosed to date) were discovered by virtue of their homol. with a known cardiac channel involved in long QT syndrome (KvLQT or KCNQ1, Kv7.1) and first disclosed in 1998. The involvement of KCNQ2 (Kv7.2) and KCNQ3 (Kv7.3) in a benign idiopathic neonatal epilepsy, KCNQ4 (Kv7.4) in a form of congenital deafness, and the discovery that neuronal KCNQ heteromultimers were among the mol. substrates of M-channels, resulted in a high level of interest for potential drug development strategies. A number of small-mol. modulators were quickly identified, including openers or activators such as the antiepileptic drug candidate **retigabine** and the structurally-related analgesic drug flupirtine (Katadolon Asta Medica), and a group of KCNQ channel inhibitors/blockers originally developed for cognition enhancement. All of these data have suggested a rich target profile for modulators of neuronal KCNQ channels, including a variety of neuronal hyperexcitability disorders and conditions for openers, such as the epilepsies, acute **pain**, neuropathic **pain**, migraine **pain** and some neurodegenerative and psychiatric disorders. KCNQ blockers could likewise have utility in disorders characterised by neuronal hypoactivity, including cognition enhancement and perhaps disorders of mood. Emerging patent literature suggests significant interest in neuronal KCNQ modulation in the pharmaceutical industry and significant chemical diversity concerning KCNQ modulation.
REFERENCE COUNT: 100 THERE ARE 100 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 28 USPATFULL on STN
ACCESSION NUMBER: 2002:34456 USPATFULL

TITLE: Methods for modulating bladder function
INVENTOR(S): Argentieri, Thomas Michael, Yardley, PA, United States
Sheldon, Jeffrey Howard, Trappe, PA, United States
Bowlby, Mark R., Richboro, PA, United States
PATENT ASSIGNEE(S): American Home Products Corporation, Madison, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6348486	B1	20020219	
APPLICATION INFO.:	US 2001-977828		20011015	(9)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2000-241078P	20001017	(60)
	US 2001-281428P	20010404	(60)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Henley, III, Raymond
LEGAL REPRESENTATIVE: Eck, Steven R.
NUMBER OF CLAIMS: 32
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 0 Drawing Figure(s); 0 Drawing Page(s)
LINE COUNT: 651
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides methods and pharmaceutical compositions for maintaining bladder control or treating urinary incontinence in a mammal utilizing agonists of KCNQ potassium channels, including KCNQ2, KCNQ3, KCNQ4 and KCNQ5 potassium channels, alone or in combination. Compounds useful in these methods include the 1,2,4-triamino-benzene derivatives described in U.S. Pat. Number 5,384,330 (Dieter et al.) and the substituted 3-phenyl oxindole compounds described in U.S. Pat. Number 5,565,483 (Hewawasam et al.). Among the preferred compounds of this invention is N-[2-amino-4-(4-fluorobenzylamino)-phenyl]carbamic acid ethyl ester, also referred to as **retigabine**.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 15 OF 28 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2002330231 EMBASE
TITLE: New pharmacological strategies for **pain** relief.
AUTHOR: Gillen C.; Maul C.
CORPORATE SOURCE: Dr. C. Gillen, Molecular Pharmacology, Gruenenthal GmbH, Zieglerstr. 6, 52078 Aachen, Germany. Clemens.gillen@grunenthal.edu
SOURCE: Expert Review of Neurotherapeutics, (2002) 2/5 (691-702). Refs: 67
ISSN: 1473-7175 CODEN: ERNXAR
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Persistent or chronic **pain** is the primary reason people seek medical advice. Despite major advances in the neurobiology of **pain**, many patients with chronic **pain** still remain insufficiently relieved. The urgent medical need for novel and safe analgesics with high efficacy has led to intense research for new targets and we want to give a comprehensive overview on the current strategies in molecular **pain** research. The recently-discovered or re-evaluated targets that yielded

compounds in clinical development will be summarized. In addition, we want to present emerging molecular strategies for **pain** relief, along with a mechanism-based classification of **pain** as the underlying concept for future diagnosis and therapy of chronic **pain**.

L4 ANSWER 16 OF 28 USPATFULL on STN

ACCESSION NUMBER: 2004:7342 USPATFULL

TITLE: Proteins and nucleic acids encoding same

INVENTOR(S): Guo, Xiaojia (Sasha), Branford, CT, UNITED STATES
Li, Li, Branford, CT, UNITED STATES
Patturajan, Meera, Branford, CT, UNITED STATES
Shimkets, Richard A., Guilford, CT, UNITED STATES
Casman, Stacie J., North Haven, CT, UNITED STATES
Malyankar, Uriel M., Branford, CT, UNITED STATES
Tchernev, Velizar T., Branford, CT, UNITED STATES
Vernet, Corine A., North Branford, CT, UNITED STATES
Spytek, Kimberly A., New Haven, CT, UNITED STATES
Shenoy, Suresh G., Branford, CT, UNITED STATES
Alsobrook, John P., II, Madison, CT, UNITED STATES
Edinger, Schlomit, New Haven, CT, UNITED STATES
Peyman, John A., New Haven, CT, UNITED STATES
Stone, David J., Guilford, CT, UNITED STATES
Ellerman, Karen, Branford, CT, UNITED STATES
Gangolli, Esha A., Madison, CT, UNITED STATES
Boldog, Ferenc L., North Haven, CT, UNITED STATES
Colman, Steven D., Guilford, CT, UNITED STATES
Eisen, Andrew, Rockville, MD, UNITED STATES
Liu, Xiaohong, Lexington, MA, UNITED STATES
Padigaru, Muralidhara, Branford, CT, UNITED STATES
Spaderna, Steven K., Berlin, CT, UNITED STATES
Zerhusen, Bryan D., Branford, CT, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004005576	A1	20040108
APPLICATION INFO.:	US 2002-231913	A1	20020830 (10)

RELATED APPLN. INFO.: Continuation of Ser. No. US 2001-10680, filed on 6 Dec 2001, PENDING

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-251660P	20001206 (60)
	US 2001-260326P	20010108 (60)
	US 2001-318712P	20010912 (60)
	US 2000-255029P	20001212 (60)
	US 2001-263800P	20010124 (60)
	US 2001-286183P	20010424 (60)
	US 2001-269942P	20010220 (60)
	US 2001-313627P	20010820 (60)

DOCUMENT TYPE: Utility

FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: MINTZ, LEVIN, COHN, FERRIS, GLOVSKY, AND POPEO, P.C., ONE FINANCIAL CENTER, BOSTON, MA, 02111

NUMBER OF CLAIMS: 41

EXEMPLARY CLAIM: 1

LINE COUNT: 17887

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed are polypeptides and nucleic acids encoding same. Also disclosed are vectors, host cells, antibodies and recombinant methods for producing the polypeptides and polynucleotides, as well as methods for using same.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 17 OF 28 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2004:134964 BIOSIS
DOCUMENT NUMBER: PREV200400137120
TITLE: **Retigabine** hyperpolarises rat dorsal root ganglion cells and reduces excitability by activation of KCNQ channels.
AUTHOR(S): Herrik, Kjartan Frisch [Reprint Author]; Jensen, Henrik Sindal [Reprint Author]; Stroebaek, Dorte [Reprint Author]; Jensen, Bo Skaaning [Reprint Author]; Christophersen, Palle [Reprint Author]
CORPORATE SOURCE: NeuroSearch, Ballerup, Denmark
SOURCE: Biophysical Journal, (January 2004) Vol. 86, No. 1, pp. 532a. print.
Meeting Info.: 48th Annual Meeting of the Biophysical Society. Baltimore, MD, USA. February 14-18, 2004. Biophysical Society.
ISSN: 0006-3495 (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Mar 2004
Last Updated on STN: 10 Mar 2004

AB In neuropathic **pain**, dorsal root ganglion (DRG) neurons may shift activity pattern from the normally silent phenotype driven by sensory inputs to a spontaneous active type responsible for ectopic input to **pain** centers in the CNS. Increasing the resting K+-conductance in DRG could dampen such activity. KCNQ2-5 channels are voltage-activated potassium channels active below the action potential threshold and potentially important for excitability regulation. Furthermore, the KCNQ channel activator, **retigabine**, shows effect in rat models of chronic **pain**. Using whole-cell patch clamp and real-time RT-PCR we investigated whether expression and function of KCNQ channels in isolated DRG from normal embryonic (eDRG) and adult rats (aDRG) may, at least partly, explain the analgesic effect of **retigabine**. Spontaneously active, cultured DRG cells firing APs at a constant rate were rarely observed (1 of 202 eDRG) although more frequently in aDRGs (5 of 45 cells). **Retigabine** (10 uM) reversibly silenced these cells by hyperpolarization. Likewise, current-evoked single APs were ameliorated. The effect was quantified by concentration-response experiments in the low uM concentration range and both capsaicin sensitive as well as insensitive cells responded to **retigabine**. XE-991 (30 uM), a selective KCNQ blocker, completely reversed the effect, as did TEA in the concentration range of 1-10 mM. In voltage-clamp, **retigabine** left-shifted the zero-current potential and increased the zero-current conductance, indicating augmented potassium conductance. In some cells **retigabine** clearly activated currents with M-channel characteristics. Real time RT-PCR studies with acutely dissociated DRG showed most prominent mRNA signal from KCNQ2, but all subtypes were detected. KCNQ2 and KCNQ3 were downregulated in adult rat DRG leaving KCNQ4 and KCNQ5 as the most frequent. These studies indicate expression and functional importance of KCNQ channels in rat DRG verifying KCNQ-channels as important **pain** targets.

L4 ANSWER 18 OF 28 USPATFULL on STN
ACCESSION NUMBER: 2002:206680 USPATFULL
TITLE: Methods of treating anxiety disorders
INVENTOR(S): Bowlby, Mark R., Richboro, PA, UNITED STATES
Rosenzweig-Lipson, Sharon J., East Brunswick, NJ, UNITED STATES
PATENT ASSIGNEE(S): American Home Products Corporation, Madison, NJ (U.S. corporation)

NUMBER KIND DATE

PATENT INFORMATION:	US 2002111379	A1	20020815
	US 6589986	B2	20030708
APPLICATION INFO.:	US 2001-22579	A1	20011217 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-256834P	20001220 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: WYETH, FIVE GIRALDA FARMS, MADISON, NJ, 07940
NUMBER OF CLAIMS: 7
EXEMPLARY CLAIM: 1
LINE COUNT: 336
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention provides methods for treating, preventing or inhibiting anxiety, anxiety-related conditions and phobias in a mammal using compounds of the formula: ##STR1##

wherein: R.sub.1 is H, alkyl, alkanoyl or the radical Ar; R.sub.2 is H or alkyl; R.sub.3 is alkoxy, NH.sub.2, alkylamino, dialkylamino, amino substituted by the radical Ar, alkyl, alkenyl, alkynyl, or the radicals Ar or ArO--; R.sub.4 is H, alkyl or the radical Ar; R.sub.5 is H or alkyl or the radical Ar; or a pharmaceutically acceptable salt or ester form thereof; Ar is an optionally substituted phenyl radical; and n is 0 or 1, or a pharmaceutically acceptable salt or ester form thereof, with the methods particularly including the use of N-[2-amino-4-(4-fluorobenzylamino)-phenyl]carbamic acid ethyl ester, also known as **retigabine**.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 19 OF 28 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2004147403 EMBASE
TITLE: Neuropathic **Pain**: Drug Targets for Current and Future Interventions.
AUTHOR: Smith P.A.
CORPORATE SOURCE: Dr. P.A. Smith, Department of Pharmacology, University of Alberta, 9.75 Medical Sciences Building, Edmonton, Alta. T6G 2H7, Canada. peter.a.smith@ualberta.ca
SOURCE: Drug News and Perspectives, (2004) 17/1 (5-17).
Refs: 188
ISSN: 0214-0934 CODEN: DNPEED
COUNTRY: Spain
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Nociceptive **pain** alerts the body to potential or actual tissue damage. By contrast, neuropathic **pain**, which results from injury or damage to the nervous system, persists long after all signs of the original injury have disappeared. This type of maladaptive **pain** presents a significant clinical problem, as it responds poorly or unpredictably to classical analgesics. There is also no single, uniformly well-tolerated drug that is reliably helpful. Current understanding of the etiology of neuropathic **pain** reveals seven potential targets for therapeutic intervention. These are: 1) ectopic activity in damaged peripheral nerves; 2) increased excitability in spinal dorsal horn neurons; 3) restoration or augmentation of GABAergic inhibition in the dorsal horn; 4) supraspinal and affective mechanisms; 5) alterations in the sympathetic nervous system; 6) spinal peptidergic mechanisms; and 7)

spinal excitatory amino acid receptors. Current therapeutic approaches, using drugs such as gabapentin, anticonvulsants, ketamine or methadone, and potential new approaches are discussed in the context of these seven drug targets. .COPYRGT. 2004 Prous Science. All rights reserved.

L4 ANSWER 20 OF 28 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2002148550 EMBASE
TITLE: Anticonvulsants for the management of **pain**.
AUTHOR: Chong M.S.; Smith T.E.
CORPORATE SOURCE: M.S. Chong, Department of Neurology, King's College Hospital, Mapother House, De Crespigny Park, London SE5 9AZ, United Kingdom. mschong@doctors.org.uk
SOURCE: Pain Reviews, (2000) 7/3-4 (129-149).
Refs: 214
ISSN: 0968-1302 CODEN: PAREFV
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 008 Neurology and Neurosurgery
024 Anesthesiology
037 Drug Literature Index
038 Adverse Reactions Titles
050 Epilepsy
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The development of anticonvulsant drugs is an example of where advances in basic neuroscience have improved patient care. Potential benefits also spill over to nonepileptic patients, especially those with chronic **pain**. It is increasingly recognized that there are many similarities between the molecular pathophysiology of epileptogenesis and that of chronic **pain**. Anticonvulsant drugs are now used extensively for treating neuropathic and non-neuropathic **pain** syndromes. This article summarizes the presumed modes of action of commonly used anticonvulsant drugs and points out where they may be important for treating **pain**. The clinical evidence for their efficacy is examined. In addition, some anticonvulsant drugs that are under development are assessed and those that may be effective for treating **pain** are highlighted.

L4 ANSWER 21 OF 28 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2003332017 EMBASE
TITLE: Adjunct agents in **pain** management: Anticonvulsants in the management of **pain**.
AUTHOR: Khan T.
CORPORATE SOURCE: T. Khan, Department of Anesthesiology, Emory University, Atlanta, GA, United States
SOURCE: Progress in Anesthesiology, (2003) 17/12 (183-202).
Refs: 316
ISSN: 0891-5784 CODEN: PRANDM
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 008 Neurology and Neurosurgery
024 Anesthesiology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English

L4 ANSWER 22 OF 28 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 2003:326545 BIOSIS
DOCUMENT NUMBER: PREV200300326545
TITLE: FLUPIRTINE A POSITIVE MODULATOR OF HETEROMERIC KCNQ2/Q3 CHANNELS.
AUTHOR(S): Ilyin, V. I. [Reprint Author]; Carlin, K. P. [Reprint

Author]; Hodges, D. D. [Reprint Author]; Robledo, S. [Reprint Author]; Woodward, R. M. [Reprint Author]
CORPORATE SOURCE: Discovery Research, Purdue Pharma L P, Cranbury, NJ, USA
SOURCE: Society for Neuroscience Abstract Viewer and Itinerary Planner, (2002) Vol. 2002, pp. Abstract No. 758.10. http://sfn.scholarone.com. cd-rom.
Meeting Info.: 32nd Annual Meeting of the Society for Neuroscience. Orlando, Florida, USA. November 02-07, 2002. Society for Neuroscience.
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Jul 2003
Last Updated on STN: 16 Jul 2003

AB KCNQ genes encode a group of potassium channels widely expressed in excitable tissues. Recent reports indicate that KCNQ2/3 heteromeric channels may underlie the native M-current in the CNS. KCNQ channels display slow activation and deactivation and little if any inactivation. Because a portion of these channels are open at normal resting membrane potentials, these channels suppress spike generation, making them potential targets for modulating activity in **pain** pathways. Flupirtine is a marketed analgesic whose mechanism of action is poorly defined. Because of the structural similarities between flupirtine and known KCNQ channel modulators we sought to determine if flupirtines analgesic activity could be mediated by KCNQ channels. We tested flupirtine side-by-side with **retigabine**, a known positive modulator of KCNQ channels. Using whole-cell patch clamp recordings from HEK-293 cells transiently transfected with KCNQ2/KCNQ3 constructs we determined that flupirtine is a positive modulator of KCNQ channels with a mechanism of action similar to that of **retigabine**. Application of flupirtine (10 uM) leads to an increase in current amplitude, a hyperpolarizing shift in the activation curve (-16+3mV) and an approximately 2 fold slowing of the deactivation kinetics. Flupirtine was a less potent modulator of KCNQ2/KCNQ3 channels than **retigabine**. In the rat Chung model of neuropathic **pain** flupirtine was equipotent to **retigabine** in reducing tactile allodynia but was less efficacious. We conclude that flupirtines effectiveness as an analgesic may be due, at least in part, to the positive modulation of KCNQ channels.

L4 ANSWER 23 OF 28 USPATFULL on STN
ACCESSION NUMBER: 2002:338226 USPATFULL
TITLE: Bisarylamines as potassium channel openers
INVENTOR(S): Andrew McNaughton-Smith, Grant, Morrisville, NC, UNITED STATES
Salvatore Amato, George, Cary, NC, UNITED STATES
PATENT ASSIGNEE(S): ICAgen, Inc., Durham, NC, 27703 (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2002193597	A1	20021219	
	US 6593349	B2	20030715	
APPLICATION INFO.:	US 2002-95617	A1	20020311	(10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-277329P	20010319 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: TOWNSEND AND TOWNSEND AND CREW, LLP, TWO EMBARCADERO CENTER, EIGHTH FLOOR, SAN FRANCISCO, CA, 94111-3834
NUMBER OF CLAIMS: 65
EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 11 Drawing Page(s)
LINE COUNT: 1810
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds, compositions and methods are provided which are useful in the treatment of diseases through the modulation of potassium ion flux through voltage-dependent potassium channels. More particularly, the invention provides bisarylamines, compositions and methods that are useful in the treatment of central or peripheral nervous system disorders (e.g., migraine, ataxia, Parkinson's disease, bipolar disorders, trigeminal neuralgia, spasticity, mood disorders, brain tumors, psychotic disorders, myokymia, seizures, epilepsy, hearing and vision loss, Alzheimer's disease, age-related memory loss, learning deficiencies, anxiety and motor neuron diseases) and as neuroprotective agents (e.g., to prevent stroke and the like) by opening potassium channels associated with the onset or recurrence of the indicated conditions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 24 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:213191 CAPLUS
TITLE: Pharmacological characterization of acid-induced muscle allodynia in rats
AUTHOR(S): Nielsen, Alexander Norup; Mathiesen, Claus; Blackburn-Munro, Gordon
CORPORATE SOURCE: NeuroSearch A/S, Department of Pharmacology, Ballerup, DK-2750, Den.
SOURCE: European Journal of Pharmacology (2004), 487(1-3), 93-103
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Previous studies have shown that repeated injections of acidic saline, given into the lateral gastrocnemius muscle of rats, results in a bilateral reduction in withdrawal threshold to tactile stimulation of the hindpaws. We have now characterised this model of muscoskeletal **pain** pharmacol., by evaluating the antinociceptive effects of various analgesics after systemic administration. The μ-opioid receptor agonist morphine (3 and 6 mg/kg) produced a particularly prolonged antiallodynic effect. The glutamate receptor antagonists ([8-methyl-5-(4-(N,N-dimethylsulfamoyl)phenyl)-6,7,8,9,-tetrahydro-1H-pyrrolo[3,2-h]-iso-quinoline-2,3-dione-3-O-(4-hydroxybutyric acid-2-yl)oxime] NS1209 and ketamine (6 and 15 mg/kg, resp.), the KCNQ K+ channel openers **retigabine** and flupirtine (10 and 20 mg/kg, resp.) and the Na+ channel blocker mexiletine (37.5 mg/kg) also significantly increased paw withdrawal threshold, although to a lesser degree than morphine. In contrast, the anticonvulsant lamotrigine (30 mg/kg), the cyclooxygenase-2 inhibitor carprofen (15 mg/kg) and the benzodiazepine diazepam (3 mg/kg) were ineffective. All antinociceptive effects were observed at nonataxic doses as determined by the rotarod test. These results suggest that in this model, muscle-mediated **pain** can be alleviated by various analgesics with differing mechanisms of action, and that once established ongoing inflammation does not appear to contribute to this process.
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 25 OF 28 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2003040622 EMBASE
TITLE: Therapeutic potential of potassium channel modulators for CNS disorders.

AUTHOR: Clark A.G.; Booth S.E.; Morrow J.A.
CORPORATE SOURCE: A.G. Clark, Lead Discovery Pharmacology, Organon Laboratories Ltd., Newhouse, Lanarkshire ML1 5SH, United Kingdom. a.clark@organon.co.uk
SOURCE: Expert Opinion on Therapeutic Patents, (1 Jan 2003) 13/1 (23-32).
Refs: 49
ISSN: 1354-3776 CODEN: EOTPEG
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Potassium (K(+)) channels play a pivotal role in the CNS, controlling cell excitability thereby raising their therapeutic application. In realisation of the utility of K(+) channels, many pharmaceutical companies have developed a plethora of antagonists and openers for a range of disorders, including stroke, epilepsy, **pain** and cognition. The most promising targets, including BK(Ca,) SK(Ca) and KCNQ channels, will be reviewed in this article. The focus will be upon the most recent K(+) channel modulator patents for CNS disorders and future developments of drugs for the treatment of CNS disorders.

L4 ANSWER 26 OF 28 USPATFULL on STN
ACCESSION NUMBER: 2002:323169 USPATFULL
TITLE: 2, 4-disubstituted pyrimidine-5-carboxamide derivatives as KCNQ potassium channel modulators
INVENTOR(S): Hewawasam, Piyasena, Middletown, CT, UNITED STATES
Dodd, Dharmpal S., Princeton, NJ, UNITED STATES
Weaver, Charles D., Wallingford, CT, UNITED STATES
Dextraze, Pierre, Laprairie, CANADA
Gribkoff, Valentin K., Wallingford, CT, UNITED STATES
Kinney, Gene G., Collegeville, PA, UNITED STATES
Dworetzky, Steven I., Middlefield, CT, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002183335	A1	20021205
APPLICATION INFO.:	US 2002-75521	A1	20020214 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-269800P	20010220 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: STEPHEN B. DAVIS, BRISTOL-MYERS SQUIBB COMPANY, PATENT DEPARTMENT, P O BOX 4000, PRINCETON, NJ, 08543-4000
NUMBER OF CLAIMS: 6
EXEMPLARY CLAIM: 1
LINE COUNT: 1346
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB There is provided a method of treatment for disorders responsive to the modulation of KCNQ potassium channels by administering to a mammal in need thereof a therapeutically effective amount of a 2,4-disubstituted pyrimidine-5-carboxamide derivative of the Formula I ##STR1##

wherein R.sup.1, R.sup.2, R.sup.3, R.sup.4 and R.sup.5 are as defined below. The present invention also provides pharmaceutical compositions comprising openers or activators of the KCNQ potassium channels and especially to the method of treatment of disorders sensitive to KCNQ potassium channel opening activity such as migraine.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 27 OF 28 USPATFULL on STN
ACCESSION NUMBER: 2002:276113 USPATFULL
TITLE: Fluoro oxindole derivatives as modulators if KCNQ potassium channels
INVENTOR(S): Hewawasam, Piyasena, Middletown, CT, United States
Dextraze, Pierre, Laprairie, CANADA
Gribkoff, Valentin K., Wallingford, CT, United States
Kinney, Gene G., Collegeville, CT, United States
Dworetzky, Steven I., Middlefield, CT, United States
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, Princeton, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6469042	B1	20021022	
	US 2002156120	A1	20021024	
APPLICATION INFO.:	US 2002-75522		20020214	(10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-270112P	20010220 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Lambkin, Deborah C.
ASSISTANT EXAMINER: Shiau, Rei-Tsang
LEGAL REPRESENTATIVE: Algieri, Aldo A.
NUMBER OF CLAIMS: 12
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 0 Drawing Figure(s); 0 Drawing Page(s)
LINE COUNT: 1133
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB There is provided novel 3-fluoro-3-phenyl oxindole derivatives of Formula I ##STR1##

wherein

R.sup.1, R.sup.2, R.sup.3 and R.sup.4 each are independently hydrogen, C.sub.1-4 alkyl, halogen, fluoromethyl, trifluoromethyl, phenyl, 4-methylphenyl or 4-trifluoromethylphenyl;

R.sup.5 is C.sub.1-6 alkyl optionally substituted with one to three same or different groups selected from fluoro and chloro, provided R.sup.5 is not C.sub.1-6 alkyl when Y is O;

Y is O or S; and

R.sup.6 and R.sup.7 each are independently hydrogen, chloro, bromo or trifluoromethy;

which are openers of the KCNQ potassium channels and are useful in the treatment of disorders which are responsive to the opening of the KCNQ potassium channels.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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SUMMARY LANGUAGE: English
AB The second article in this month's special feature discusses current anti-epileptic drugs, looks ahead to possible therapeutic developments and emphasises the opportunities for clinical pharmacists to improve medicines management in patients with epilepsy.